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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/618,320	07/11/2003	Yasuhiko Takahashi	600630-7US (562399)	8239

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EXAMINER	
TURNER, SHARON L	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 05/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/618,320	TAKAHASHI ET AL.	
	Examiner	Art Unit	
	Sharon L. Turner	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-53* is/are pending in the application.

4a) Of the above claim(s) *1-6,9-12,18-22 and 25-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,8,13-17,23 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-53* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2-24-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group II, polynucleotides and the sequence of SEQ ID NO:1 in the reply filed on 2-14-06 is acknowledged. The traversal is on the ground(s) that the nucleotide of SEQ ID NO:2 encodes SEQ ID NO:1, that claims 52 is dependent on claim 49 and that groups IX-XV are suitably related. This is not found persuasive because the search and examination of the different groups is non-coextensive in scope and are separable as set forth in the restriction requirement. The Examiner does acknowledge the case law of Ochiai and Brouwer. However, rejoinder is not applicable until the indication of allowable subject matter. The dependency of the claims is noted but is not co-extensivie with the elected subject matter.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-6, 9-12, 18-22, 25-53 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2-14-06.

Claim Objections

3. Claims 7-8, 13-17, and 23-24 are objected to because of the following informalities:

The claims are directed in part to non-elected subject matter and/or SEQ ID NO's. Search is limited to the elected SEQ ID NO. Claims 15-17 are further objected to as being drawn to non-elected transgenics. The host cell should be stipulated as "isolated". Appropriate correction is required.

Priority

4. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a translation of the foreign application should be submitted under 37 CFR 1.55 in reply to this action.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 7-8, 13-17, and 23-24 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial, credible asserted utility or a well established utility.

The specification discloses only that the instant nucleic acids constitute a family member of a g-protein coupled receptor. However, the specification does not set forth the particular receptor, its structure, function and significance such that one of skill in the art is provided either a specific and substantial asserted utility or a well established utility. While the specification contemplates the use of the disclosed nucleic acids for preparation of probes and primers for use in hybridizations and PCR amplifications, production of proteins and mRNAs encoded by said sequences as well as related nucleic acids, methods to identify compounds that bind and/or inhibit, the specification offers no specific evidence or examples to place significance on the particular function

and use of the claimed compounds. The asserted utilities are not either specific or substantial because these uses merely rely on the inherent properties of any nucleic acid to hybridize (bind) and encode. Thus, the disclosed nucleic acids merely constitute research reagents for further experimentation to discover a "real-world" use of the nucleic acids. As recognized by Skolnick et al., Trends in Biotech., 18(1):34-39, 2000 the skilled artisan is well aware that there is an unpredictable nature in the ability of encoding nucleic acids to predict structural and functional activities for any particular protein or protein family, and that even when highly homologous and conserved residues are known only experimental research can confirm the artisan's best guess, see in particular Skolnick, abstract and Box 2. In addition G-protein coupled receptors are a broad class of receptors known to differ substantially in structure and function. The mere assertion that the claimed sequences correspond to a G-protein is not significant to establish a specific and substantial, use, significance function and/or effect. As further delineated below even single amino acid exchanges may obviate function for even the most homologus of sequences in this broad class. G-proteins are a broad class of receptors. Receptor function, however, cannot be reliably predicted from protein sequence homology. For example, Transforming Growth Factor (TGF-beta) Family OP-1 induces metanephrongenesis whereas closely related TGF-beta family members-BMP-2 and TGF-beta1-have no effect on metanephrogenesis under identical conditions (Vukicevic et al., 1996, PNAS USA 93:9021-9026). Platelet-derived Growth Factor (PDGF) Family VEGF, a member of the PDGF family, is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells while PDGF is mitogenic for

vascular smooth muscle cells but not for vascular endothelial cells (Tischer et al., U.S. Patent 5,194,596, column 2, line 46 to column 3, line 2). Finally, vertebrate growth hormone of 198 amino acids becomes an antagonist (inhibitor of growth) when a single amino acid is changed (Kopchick et al, U.S. Patent No. 5,350,836). Even 99% homology does allow predictability in this instance. Given the unpredictability of homology comparisons, and the fact that the specification fails to provide objective evidence that the additional sequences are indeed species of the claimed genus it cannot be established that a representative number of species have been disclosed to support the genus claim. No activity is set forth for the additional sequences. Accordingly, the claimed invention lacks compliance with the utility requirement and the specification lacks adequate written description support for the broad class of molecules and fails to teach the artisan how to make and use the invention in commensurate scope with the claims.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 7-8, 13-17, and 23-24 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial, credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

In addition to the aforementioned, the following defects are noted with respect to enablement and written description of the instant invention as claimed.

The specification describes a polypeptide sequence consisting of SEQ ID NO:1 encoded by SEQ ID NO:2, which is asserted to be a g protein coupled receptor. However, the specification fails to evidence the specific function, significance or any specific and substantial utility for the noted peptide sequence. In addition, the claims as written include polypeptides comprising fragments and homologues, encompass polypeptides that vary substantially in length and also in amino acid composition. The instant disclosure of a single polypeptide, that of SEQ ID NO:1 with no disclosed specific activity, does not adequately support the scope of the claimed genus of polynucleotides encompassed which share no discernible similar structure, utility or significance and which encompasses a substantial variety of subgenera. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, a single isolated polypeptide sequence SEQ ID NO: 1 and no other amino acid sequences that are proposed to possess the same activity as SEQ ID NO: 1 based solely on homology considerations.

As previously discussed G-protein receptor function cannot be reliably predicted from protein sequence homology. For example, Transforming Growth Factor (TGF-beta) Family OP-1 induces metanephrongenesis whereas closely related TGF-beta family members-BMP-2 and TGF-beta1-have no effect on metanephrogenesis under identical conditions (Vukicevic et al., 1996, PNAS USA 93:9021-9026). Platelet-derived Growth Factor (PDGF) Family VEGF, a member of the PDGF family, is mitogenic for vascular

endothelial cells but not for vascular smooth muscle cells while PDGF is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (Tischer et al., U.S. Patent 5,194,596, column 2, line 46 to column 3, line 2). Finally, vertebrate growth hormone of 198 amino acids becomes an antagonist (inhibitor of growth) when a single amino acid is changed (Kopchick et al, U.S. Patent No. 5,350,836). Even 99% homology does allow predictability in this instance. Given the unpredictability of homology comparisons, and the fact that the specification fails to provide objective evidence that the additional sequences are indeed species of the claimed genus it cannot be established that a representative number of species have been disclosed to support the genus claim. No activity is set forth for the additional sequences.

Further, the specification is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors relevant to this discussion include the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims.

Applicants claims are directed to peptides with greater than single amino acid substitutions, naturally occurring variants, biologically active peptide fragments and homologues.

The specification does not enable the broad scope of the claims which encompasses a multitude of analogs or equivalents because the specification does not teach which residues can or should be modified such that requisite functionality is maintained, note utility rejection above. The specification provides essentially no guidance as to which of the essentially infinite possible choices is likely to be successful in any particular use and the skilled artisan would not expect functional conservation amongst homologous sequences. Thus, applicants have not provided sufficient

guidance to enable one skilled in the art to make and use the claimed derivatives in a manner reasonably correlated with the scope of the claims.

The skilled artisan recognizes that nucleic and amino acid alterations may lead to differences in function. For example, the skilled artisan recognizes as noted in Skolnick et al., above and as further exemplified by Choh, PNAS 77(6):3211-14, 1990, that one or more amino acid deletions, insertions or substitutions including truncations results in unpredictable effects in the resulting biological molecule, its' biological function, the ability to bind and/or exhibit similar immunoreactivity. The specification teaches no structural or functional activities of the protein or nucleic acid, fails to teach any residues which may be exchanged while retaining requsite activity or function and fail to teach the significance or function of any particular variants. As to the nucleic acids, the skilled artisan recognizes that encoding nucleic acids are dependent upon the structural nucleotides and their relationship to the genetic code and translational signals. The specification fails to note those nucleic acid molecules that are capable of encoding the requisite peptides sharing either structure and/or function. As noted above, the peptide structures and their pertinent sequences are insufficiently disclosed and/or enabled to the full scope of the claim.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986). Thus, the skilled artisan cannot readily make and use the claimed sequences without further undue experimentation.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claim 7, 13-17, 23-24 are rejected under 35 U.S.C. 102(e) as being anticipated by WO200175067, Drmanac et al., 11 Oct. 2001 (IDS 2-24-04). The reference particularly teaches agents corresponding to polynucleotides corresponding to nucleic acids encoding amino acids 96-126 of SEQ ID NO:1 as set forth below, with carrier, as recombinant vector, in host cells and utilization to produce peptide. Accordingly the reference teachings anticipate the claimed invention.

ABG01236
ID ABG01236 standard; protein; 461 AA.
AC ABG01236;
DT 13-FEB-2002 (first entry)
DE Novel human diagnostic protein #1227.
KW Human; chromosome mapping; gene mapping; gene therapy; forensic;
KW food supplement; medical imaging; diagnostic; genetic disorder.
OS Homo sapiens.
PN WO200175067-A2.
PD 11-OCT-2001.
PF 30-MAR-2001; 2001WO-US008631.
PR 31-MAR-2000; 2000US-00540217.
PR 23-AUG-2000; 2000US-00649167.
PA (HYSE-) HYSEQ INC.

PI Drmanac RT, Liu C, Tang YT;
DR WPI; 2001-639362/73.
DR N-PSDB; AAS65423.
PT New isolated polynucleotide and encoded polypeptides, useful in
PT diagnostics, forensics, gene mapping, identification of mutations
PT responsible for genetic disorders or other traits and to assess
PT biodiversity.
PS Claim 20; SEQ ID NO 31595; 103pp; English.
CC The invention relates to isolated polynucleotide (I) and polypeptide (II)
CC sequences. (I) is useful as hybridisation probes, polymerase chain
CC reaction (PCR) primers, oligomers, and for chromosome and gene mapping,
CC and in recombinant production of (II). The polynucleotides are also used
CC in diagnostics as expressed sequence tags for identifying expressed
CC genes. (I) is useful in gene therapy techniques to restore normal
CC activity of (II) or to treat disease states involving (II). (II) is
CC useful for generating antibodies against it, detecting or quantitating a
CC polypeptide in tissue, as molecular weight markers and as a food
CC supplement. (II) and its binding partners are useful in medical imaging
CC of sites expressing (II). (I) and (II) are useful for treating disorders
CC involving aberrant protein expression or biological activity. The
CC polypeptide and polynucleotide sequences have applications in
CC diagnostics, forensics, gene mapping, identification of mutations
CC responsible for genetic disorders or other traits to assess biodiversity
CC and to produce other types of data and products dependent on DNA and
CC amino acid sequences. ABG00010-ABG30377 represent novel human diagnostic
CC amino acid sequences of the invention. Note: The sequence data for this
CC patent did not appear in the printed specification, but was obtained in
CC electronic format directly from WIPO at
CC ftp.wipo.int/pub/published_pct_sequences
XX
SQ Sequence 461 AA;

Query Match 100.0%; Score 153; DB 4; Length 461;
Best Local Similarity 100.0%; Pred. No. 1.2e-12;
Matches 31; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 KEARKVSRGIDRMLRDQKRDLQQTHRLLLLG 31
||||||||||||||||||||||||||||||
Db 96 KEARKVSRGIDRMLRDQKRDLQQTHRLLLLG 126

Conclusion

11. No claims are allowed.

12. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (571) 272-0894. The examiner can normally be reached on Monday-Thursday from 7:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached at (571) 272-0867.

Sharon L. Turner, Ph.D.
April 30, 2006

SHARON TURNER, PH.D.
PRIMARY EXAMINER
4-30-06